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PAPER

Toxicology

Forensic alcohol calculations in transgender individuals undergoing gender-affirming hormonal treatment

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Abstract

There are an increasing number of individuals undergoing gender-affirming hormonal treatment (GAHT) to treat gender dysphoria. Current forensic alcohol calculations require knowledge of the sex of the individual, but this may disadvantage trans people as research has demonstrated that there are physiological changes in individuals who are undergoing GAHT. Using previously published studies on total body water (TBW) in cis individuals, and the known changes in lean body mass and hematocrit in trans individuals, it is possible to estimate TBW in trans individuals and compare them to those cis equation estimations. When using these revised rubrics, we determined that for trans women the use of the cis male anthropometric TBW equation only gives a small underestimation of TBW (0.9%) compared to the underestimation of TBW using the cis female TBW equation (-17.7%). For trans men, the use of the cis female TBW equation gives the largest disadvantage, underestimating TBW by -10.8% compared to the cis male TBW equation, that overestimates TBW by 6.6%. For this reason, we recommend that if the sex at birth of an individual is not known or disclosed, any forensic alcohol calculations in a forensic alcohol reports are made assuming that the gender declared by the individual is their sex at birth. Further research to develop validated anthropometric TBW equations are urgently needed as to not disadvantage trans people when forensic alcohol calculations are carried out.

KEYWORDS

alcohol, ethanol, forensic alcohol calculations, gender-affirming hormonal treatment, total body water, transgender

Highlights

- Large number of people taking gender-affirming hormonal treatment (GAHT) around the world.
- Total body water is altered in individuals taking GAHT.
- Forensic alcohol calculation results are affected by GAHT.
- Forensic alcohol reports should state assumption that individual is cis (unless sex at birth is known).

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1 | INTRODUCTION

Around the world there are estimated to be between 0.1% and 2% of the population who are transgender [1]. Transgender is defined as people who have a gender identity which differs from the sex they were assigned at birth (sex at birth) [1]. The antonym of transgender is cisgender which describes a person whose sex at birth and gender identity are the same. The true number of transgender individuals around the world is unclear and is most likely being underestimated due to cultural sensitivities [2]. Based on current data, around 80% of transgender individuals are either taking or want to take gender-affirming hormone therapy (GAHT) [3]. The use of GAHT aims to align the characteristics of an individual with their gender identity. GAHT transgender women commonly receive estrogen, often in conjunction with an androgen blocker or gonadotrophin-releasing hormone analogues. GAHT transgender men receive testosterone [4,5]. These treatments are known to alter the body characteristics of the individuals taking them [4,5], and these body changes may influence the results of forensic alcohol calculations that are often based on the sex of an individual rather than their gender. In forensic science, it is important to have a rigorous evidence base for forensic practices, particularly making sure that the practices do not disadvantage individuals or groups of individuals that may lead to miscarriages of justice [6]. Forensic alcohol calculations, probably the most performed forensic calculations, have a solid evidence base due to many years of research (summarized in Ref. [7]). However, as far as the authors are aware there are no published guidelines, or recommendations, for forensic alcohol calculations that take into account the body changes that occur in individuals undergoing GAHT. The United Kingdom Association of Forensic Toxicologists (UKIAFT) alcohol calculation guidelines do state that the information collected for forensic alcohol calculations should include "sex at birth" [8]. The assumption in these guidelines are that the individual undergoing GAHT will have a total body water similar to individuals of the sex they were assigned at birth. However, to date there are no studies looking at the body changes in transgender individuals with regard to forensic alcohol calculations. Additionally, depending on the legal jurisdiction, if an individual has legally changed their gender, they are under no obligation to disclose their sex at birth. The aim of this study is to investigate forensic alcohol calculations in individuals that are undergoing GAHT.

1.1 | Forensic alcohol calculations

The most common form of the equation, known as the Widmark equation, to estimate the blood alcohol concentration of an individual after consumption of a known amount of alcohol is:

$$C_o = \frac{100 \cdot A \cdot F_{water}}{TBW} \tag{1}$$

C_o - the hypothetical BAC at time zero before any metabolism has occurred (mg/100ml). A - amount of pure ethanol consumed (g). F_{water}

- fraction of blood volume that is water (% w/v). TBW - total body water of an individual (L).

For an individual undergoing GAHT, there will be various physiological changes to their body. In the case of forensic alcohol calculations, the two variables that are likely to be altered by GAHT therapy are TBW and F_{water} .

1.2 | Total body water (TBW) and gender-affirming hormonal treatment (GAHT)

There have been a number of studies looking at the changes of both body fat and fat-free mass in individuals undergoing GAHT. These studies have shown that on average, following the commencement of GAHT in trans women, there is an increase in body weight, an increase in body fat, and a decrease in lean body mass [9]. On average, in trans men, there is a decrease in body weight, decrease in body fat, and an increase in lean body mass following the commencement of GAHT [9]. The variable of importance here for forensic alcohol calculations is that of lean body mass. Lean body mass is proportional to TBW , as the water content of the tissues is considered a constant [10,11]. Thus, if the changes of lean body mass following GAHT are known, the changes in TBW after GAHT can be estimated. The revised TBW in transgender individuals can then be utilized in forensic alcohol calculations. In a meta-analysis of individuals undergoing GAHT, lean body mass was observed in trans women, on average, to decrease by -2.44 kg (-2.76 to -2.11 kg; 95% CI), and on average, to increase in trans men by 3.87 kg (3.22-4.53 kg; 95% CI) [9]. In a study of 179 trans women and 162 trans men 1 year (12 months) after commencement of GAHT, lean body mass had decreased by -3% [-4 to -2%; 95% CI] in trans women and increased by +10% [9%-11%; 95% CI] in trans men [12]. Thus, the mean change in TBW for trans men would be approximately +10% and approximately -3% in trans women (Figure 1).

1.3 | Percentage of blood that is water (F_{water}) and gender-affirming hormonal treatment (GAHT)

Forensic alcohol calculations to determine the blood alcohol concentration of an individual after consuming a known amount of ethanol rely on not only the estimation of the individuals TBW , but also F_{water} . Taking into account any potential changes in the

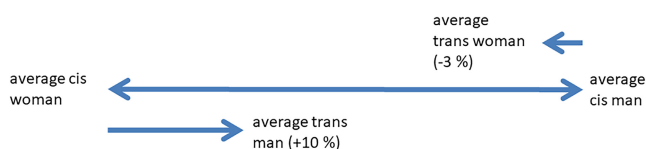


FIGURE 1 Mean percentage differences in total body water between cis men and cis women and the percentage change in total body water in trans people following gender-affirming hormone therapy [Color figure can be viewed at wileyonlinelibrary.com]

percentage of blood that is water in people undergoing GAHT is also important. To date no studies have been directly carried out on the individuals undergoing GAHT and their F_{water} , however previous work has demonstrated that whole blood water (WBW) correlates ($r = -0.96$) with hematocrit (Hct) [13,14] using the Equation 2.

$$\text{WBW (mass \%)} = -28.6 \times \text{Hct (v/v)} + 91.8 \quad (2)$$

If the change in Hct was known in trans individuals the change in F_{water} could then be estimated. Studies in individuals undertaking GAHT have shown that there is, on average, a decrease in hematocrit in trans women and an increase in hematocrit in trans men [15]. In a study of 239 trans women undergoing GAHT, hematocrit decreased from 45.1 Hct % [42.7–47.59 Hct %; 95% CI] at baseline to 41.0 Hct % [39.9–43 Hct %; 95% CI]; a change of -4.1 Hct % (3.50–4.37 Hct %; 95% CI) stabilizing after 3 months. In the same study looking at 192 trans men undergoing GAHT the hematocrit increased by 4.9 Hct % [3.82–5.25 Hct %; 95% CI] from 41.1 Hct % [39.0–42.6 Hct %; 95% CI] to 46.0 Hct % [44.0–47.0 Hct %; 95% CI] after 12 months [15]. After the conversion of hematocrit to WBW using Equation 2, WBW (mass %) is 80.07 for trans women and 78.64 in trans men. WBW then needs to be converted to F_{water} (%w/v) by multiplying the blood water content percentage by 1.0506, the specific gravity of blood at 37°C [16]. This gives an F_{water} of 0.841 for trans women [17] compared to 0.838 for cis (gender identity equal to sex assigned at birth) women and 0.826 for trans men compared to 0.825 for cis men [17].

TABLE 1 Changes in total lean body mass based on body mass index (BMI) of people undergoing gender-affirming hormonal treatment (GAHT) 1 year post the start of therapy. Data from Klaver et al [12]

BMI (kg/m ²)	Mean $\Delta\%$ total lean body mass (95% CI)	
	Trans women	Trans men
<20	-2 (-4; -1)	13 (11; 16)
20–25	-2 (-3; -1)	11 (9; 12)
25.1–30	-5 (-6; -3)	11 (9; 13)
>30	-4 (-6; -2)	7 (5; 9)
ALL	-3% (-4; -2)	10 (9; 11)

1.4 | Changes in total body water (TBW) in individuals undergoing gender-affirming hormone therapy (GAHT)

The studies above have shown that there are body changes that will alter the results of forensic alcohol calculations in transgender individuals when compared to cisgender individuals. The work of Klaver et al [12] demonstrated that on average, the mean change in TBW for trans men was approximately +10% and approximately -3% in trans women. As can be seen in Table 1 the actual change in lean body mass differs according to the body mass index (BMI) of the individual before the start of GAHT. In order to investigate the effects of these changes on the

TABLE 2 Mean total body water of cis men and cis women based on body mass index (BMI) based on data from Maskell et al [22]

BMI (kg/m ²)	Cis man (TBW (L))			Cis woman (TBW (L))			% difference in mean TBW in cis men compared to cis women
	mean	SD	n	mean	SD	n	
<20	36.2	4.4	15	28.9	3.4	73	25.3
20–25	43.1	5.9	271	31.6	4.3	334	36.4
25.1–30	46.9	6.1	205	33.1	4.0	238	41.7
>30	53.5	8.1	91	39.5	7.2	239	35.4
ALL	45.9	7.4	582	33.9	6.2	884	35.4

TABLE 3 Estimated mean total body water (TBW) of transgender individuals after 12 months of gender-affirming hormonal treatment (GAHT) using data from Maskell et al [22] assuming that the GAHT caused changes to TBW according to data collected by Klaver et al [12]

BMI	Trans women (TBW (L))			Trans men (TBW (L))			% Difference in mean TBW between trans women and cis women	% Difference in mean TBW between trans men and cis men	% Difference in mean TBW between trans men and trans women
	mean	SD	n	mean	SD	n			
<20	35.5	4.3	15	32.7	3.9	73	22.8	-9.7	-7.9
20–25	42.2	5.7	271	35.1	4.7	334	33.5	-18.6	-16.8
25.1–30	44.6	5.8	205	36.7	4.5	238	34.7	-21.7	-17.7
>30	51.3	7.8	91	42.3	7.7	239	29.9	-20.9	-17.5
ALL	44.3	7.0	582	37.3	6.4	884	30.7	-18.7	-15.8

estimation of TBW and C_o in transgender individuals, two data sets were utilized: (1) the cis male data ($n = 582$) and (2) the cis female data ($n = 884$). Both of these data sets are part of a clinical study from the New York Obesity Research Centre at St. Lukes-Roosevelt Hospital, New York [18,19]. These data sets are comprised of the sex at birth, height, body mass (weight), age, and total body water (measured by the ^3H -dilution method). Table 2 shows the mean ($\pm\text{SD}$) total body water ranges grouped into BMI of both cis men and cis women. Based on these data, cis males have a mean TBW of 45.9 ± 7.4 L ($n = 582$) and cis women have a mean TBW of 33.9 ± 6.2 L ($n = 884$) with a mean difference of 35.4% (~ 12 L). The measured TBW of the cis males and cis females was revised to estimate the TBW of trans individuals based on percentage changes in lean body mass based on the BMI of the cis individuals, detailed in Table 1. As can be seen in Table 3 the mean ($\pm\text{SD}$) TBW of trans women based on the starting cis male population is estimated to be 44.3 ± 7.0 L and for trans men to be 37.3 ± 6.4 L based on a starting cis female population. The only current guidance that applies to alcohol calculations in trans individuals suggests that the gender at birth should be used for ethanol calculations [8]. However, based on the data from Klaver et al [12], on average the TBW of a trans woman would be 3% lower than a cis man and 10% higher for a cis woman compared to a trans man. Overall, as shown in Table 3, there is a +30.7% difference between the average TBW of trans woman compared to the average TBW of a cis woman with a -18.7% mean difference in the average TBW of a trans man compared to the average TBW of a cis man. Although there is a change in physiological parameters (TBW) toward that of the chosen rather than assigned sex at birth, the physiological changes after undergoing GAHT are not as large as would be expected if the individual has been assigned that gender at birth.

1.5 | Revision of anthropometric equations for individuals undergoing gender-affirming hormone therapy (GAHT)

Based on the known changes to TBW in individuals undergoing GAHT, the anthropometric TBW equation of Watson et al [20] can be altered to estimate the effects of GAHT. The revised equations being:

$$\text{TBW (trans man)} = -2.097 + (0.1069 \times \text{Height}) + (0.2466 \times \text{Weight}) \times 1.1 \quad (3)$$

$$\text{TBW (trans woman)} = (2.447 - (0.09516 \times \text{Age}) + (0.1074 \times \text{Height}) + (0.3362 \times \text{Weight})) \times 0.97 \quad (4)$$

Weight (body mass in kg), age (years), height (cm).

The multiplications at the end of the trans men and trans women equations are adjusting for the mean change in TBW based on the studies above, +10% in trans men and -3% in trans women.

TABLE 4 Difference in mean TBW for transgender individuals^a when the TBW is estimated with the proposed trans gender equation compared to (a) TBW being estimated using sex at birth (cis) TBW equation or (b) TBW is estimated using the affirmed gender TBW equation

BMI	Trans women				Trans men			
	Difference in TBW between cis man and trans gender (trans woman) (L)	(a) % Difference in TBW between cis man and trans gender (trans woman) (L)	(b) % Difference in TBW between cis woman and trans gender (trans woman) (L)	(b) Difference in TBW between cis man and trans gender (trans man) (L)	(a) Difference in TBW between cis woman and trans gender (trans man) (L)	(a) % Difference in TBW between cis woman and trans gender (trans man) (L)	(b) Difference in TBW between cis man and trans gender (trans man) (L)	(b) % Difference in TBW between cis man and trans gender (trans man) (L)
<20	-0.3	-0.6	-5.5	-5.0	-14.6	-14.6	0.5	2.0
20-25	-1.6	-3.2	-8.5	-5.3	-14.2	-14.2	0.4	1.8
25.1-30	-0.3	0.0	-7.9	-4.1	-10.5	-10.5	1.9	5.6
>30	1.9	4.1	-8.2	-2.5	-5.2	-5.2	6.5	15.6
ALL	-0.6	-0.9	-8.1	-4.2	-10.8	-10.8	2.4	6.6

^aAfter 12 months of gender-affirming hormonal treatment (GAHT).

1.6 | Are trans individuals undergoing gender-affirming hormone therapy (GAHT) potentially disadvantaged by current practices?

1.6.1 Total body water

Current UKIAFT guidelines for forensic practitioners state that the individuals' total body water should be determined based on the individuals' sex at birth. Complications to this approach include that the transgender individual undergoing GAHT may have legally changed their gender and decided not to disclose their sex at birth for use in forensic alcohol calculations. This may bias the calculated result of the forensic alcohol calculation. Using the data from [18,19] we calculated the "true" mean total body water of trans men (Equation 5) and trans women (Equation 6). These data then allowed the calculation of the percentage difference in TBW if a) the cis male and b) the cis female TBW equations were used. As can be seen in Table 4 the TBW of a trans man would be underestimated by, on average, 4.2L (10.8% difference) if the cis female TBW equation was used to estimate TBW. TBW would be overestimated, on average, by 2.4L (6.6% difference) if the cis male TBW equation was used. In transwomen the TBW would be underestimated, on average, by 0.6L (0.9% difference) if the cis male TBW equation was used to estimate the individuals' TBW. TBW would be underestimated, on average, by 8.1L (17.7% difference) if the cis female TBW equation was used. These data demonstrate that trans women would be most disadvantaged if the cis female TBW anthropometric equation was used to estimate their TBW. Trans men would be most disadvantaged if the cis female anthropometric TBW equation was used to estimate their TBW.

1.7 | Estimated BAC at time zero (C_o)

It is important to determine how these differences in TBW observed in transgender individuals undergoing GAHT, described above, would alter the calculated C_o . In order to look at the differences in C_o , we used Equation 1 to calculate the C_o . This calculation used the TBW calculated above, the F_{water} of 0.838 (cis women); 0.825 (cis man); 0.841 (trans women) and 0.826 (trans men). Finally, we used two different doses of ethanol. It was assumed that an individual had consumed either 2 UK units of alcohol (16 g; $\sim 2 \times 25$ ml "shots" of 40% ABV vodka) or 10 UK units of ethanol 80 g ($\sim 1 \times 750$ ml bottle of wine, 13% ABV). Table 5 shows the calculated C_o , with Table 6 showing the mean and percentage differences in C_o between the various groups. As with the TBW the estimation of C_o in transgender women using the cis female TBW anthropometric equation would disadvantage trans women the most with a mean overestimation of C_o of ~ 7 mg/100 ml ($\sim 23\%$ difference) for a dose of 16 g of ethanol and a mean overestimation of C_o of ~ 32 mg/100 ml ($\sim 21\%$ difference) for a dose of 80 g of ethanol. For trans men, as with TBW the use of the cis female TBW equation would give the greatest disadvantage with a mean overestimation of C_o of ~ 6 mg/100 ml ($\sim 17\%$ difference) for a dose of 16 g of ethanol. For an 80 g dose of ethanol there would be a mean overestimation of C_o of ~ 26 mg/100 ml ($\sim 14\%$ difference) for trans men if the cis female calculations were used. Overall trans men would be disadvantaged to a greater extent with the use of sex at birth than trans women.

TABLE 5 Mean estimated blood alcohol concentration at time zero (C_o) after the consumption of 16 g or 80 g of ethanol (alcohol) for transgender individuals^a when (a) the sex at birth; (b) affirmed gender or (c) specific transgender calculations are used

Dose of ethanol (g)	BMI (kg/m ²)	Mean Estimated C_o (mg/100ml)					
		Trans women			Trans men		
		(a) Cis male calculation (sex at birth)	(b) Cis female calculation (male data)	(c) Trans female calculation	(a) Cis female calculation (sex at birth)	(b) Cis male calculation (female data)	(c) Trans male calculation
16	<20	38	45	38	49	40	41
	20–25	33	40	33	45	38	38
	25.1–30	30	37	31	41	35	37
	>30	25	32	27	35	28	32
	ALL	31	38	31	42	34	36
80	<20	190	225	192	243	201	205
	20–25	164	200	163	226	188	192
	25.1–30	150	184	153	207	173	183
	>30	127	158	134	172	140	161
	ALL	154	188	156	208	172	182

^aAfter 12 months of gender-affirming hormonal treatment (GAHT).

TABLE 6 Difference in mean C_0 for transgender individuals^a when the C_0 is calculated with the proposed trans gender equation compared to (a) C_0 is calculated using sex at birth (cis) or (b) C_0 is calculated using the assigned gender

		Estimated C_0 (mg/100ml)									
		Trans women					Trans men				
Dose of Ethanol (g)	BMI	Difference in C_0 trans gender (trans woman) (mg/100 ml)	(a) % Difference in C_0 between cis man and trans gender (trans woman)	(b) Difference in C_0 between cis woman and trans gender (trans woman) (mg/100 ml)	(b) % Difference in C_0 between cis woman and trans gender (trans woman)	(a) Difference in TBW between woman and trans gender (trans man) (L)	(a) % Difference in TBW between cis woman and trans gender (trans man)	(b) Difference in TBW between man and trans gender (trans man) (L)	(b) % Difference in TBW between cis man and trans gender (trans man)		
16	<20	0	0.0	7	18.4	8	19.5	-1	-2.4		
	20-25	0	0.0	7	21.2	7	18.4	0	0.0		
	25.1-30	-1	-3.2	6	19.4	4	10.8	-2	-5.4		
	>30	-2	-6.3	5	18.5	3	9.4	-4	-12.5		
	ALL	0	-0.6	7	22.6	6	16.7	-2	-5.6		
80	<20	-2	-1.0	33	17.2	38	18.5	-4	-2.0		
	20-25	1	0.8	37	22.7	34	17.7	-4	-2.1		
	25.1-30	-3	-1.8	31	20.3	24	13.1	-10	-5.5		
	>30	-7	-5.4	24	17.9	11	6.8	-21	-13.0		
	ALL	-2	-1.3	32	20.5	26	14.3	-10	-5.5		

^aAfter 12 months of gender-affirming hormonal treatment (GAHT).

1.8 | What are the implications of using the affirmed gender rather than sex at birth for individuals undergoing gender-affirming hormone treatment?

Transgender individuals undergoing GAHT who have legally changed their gender from that assigned at birth are commonly under no obligation to give their sex at birth. Ideally for trans individuals the best estimation of TBW would be to use a validated anthropometric TBW equations specific to transgender individuals. However, for trans women the use of the cis male anthropometric TBW equation only gives a small disadvantage (TBW -1% ; $C_o \sim -1\%$) compared to the cis female equation (TBW -17.7% ; $C_o \sim 22\%$). For trans men the use of the cis female TBW equation at birth gives the largest disadvantage (TBW -10.8% ; $C_o \sim 15\%$) compared to the cis male TBW equation (TBW $\sim 6.6\%$; $C_o \sim 5.5\%$). For this reason, we recommend that if the sex at birth of an individual is not known or not disclosed any forensic alcohol calculations in the report are made assuming that the gender declared by the individual is their sex at birth.

1.9 | Ethanol elimination rates

The rate of ethanol elimination is also an important parameter in forensic alcohol calculations [7]. However as the same ethanol elimination rates and ranges are used for both sexes in forensic ethanol calculations trans specific ethanol elimination rates and ranges do not need to be used [21].

1.10 | Limitations

This study is based on the mean changes that occur in TBW and F_{water} following 12 months of GAHT in trans men and trans women that are mainly Western Caucasians with an age range of 18–66. It is important to note that the trans equations given in this study are not validated and only give an estimation of the true TBW in trans individuals. It is also important to note that this study also only investigated trans individuals that have undergone at least 12 months of GAHT. In order to validate TBW water equations for use in transgender individuals, studies need to be carried out in transgender individuals of a wide range of ages, BMI, races and genders to develop anthropometric equations. Studies should also be carried out to determine the F_{water} in transgender individuals. Until these studies are carried out forensic practitioners should be aware that transgender individuals may be disadvantaged by alcohol calculations. Equations 5 and 6 may give a better estimation of TBW for trans individual than the cis equations but to date have not been validated and caution should be taken with their use. Equations 5 and 6 are however the best equations for trans individuals we have to date and should give a better reflection of the TBW of a trans individual.

2 | CONCLUSIONS

This study has demonstrated that transgender individuals that have undergone 12 months of GAHT are currently disadvantaged by the use of the present cis TBW equations. We recommend that if it is not known if the individual is cis gender or trans gender then a forensic alcohol calculation report should state the assumption that the gender given by the individual is considered to be the sex at birth. Further research to develop validated anthropometric TBW equations are urgently needed as to not disadvantage trans people when forensic alcohol calculations are carried out.

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DEFINITIONS

Sex at birth – (sex assigned at birth). Sex at birth is typically assigned based on a person's reproductive system and other physical characteristics.

Cisgender - describes a person whose gender identity and sex assigned at birth are the same.

Transgender – a person who has a gender identity or gender expression that differs from the sex that they were assigned at birth.

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